UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/936,333	03/05/2002	Robert B. Dickson	P 0280655	4097

909 7590 01/27/2005

PILLSBURY WINTHROP, LLP
P.O. BOX 10500
MCLEAN, VA 22102

EXAMINER	
LUCAS, ZACHARIAH	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 01/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/936,333	DICKSON ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- Th MAILING DATE of this communication appears on the cover sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☒ Claim(s) *1-33* is/are pending in the application.

4a) Of the above claim(s) *1-14, 20-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group V (claims 15-19, antibodies to matriptase) and to embodiments wherein the antibodies are specific to the two-chain form of matriptase in the reply filed on November 23, 2004 is acknowledged.

2. Claims 1-14, 20-33 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on November 23, 2004.

Specification

3. The disclosure is objected to because of the following informalities:

On page 10, line 10 as amended on November 23, 2004, the specification refers to the cDNA sequence of SEQ ID NO: 5. However, SEQ ID NO: 5 is a protein sequence. It is therefore unclear what is being referred to.

On page 22, lines 1-2, the application describes an epitope as a portion of an antigen molecule to which an antibody or an "immunogenic fragment thereof" binds. However, in the art, and on page 21 of the application, the term "immunogenic fragment" is understood to mean a portion of a protein that induces an immunogenic response. It is therefore unclear what is meant by the phrase "immunogenic fragment" as used on page 22, and it is suggested that the phrase "immunologically reactive fragments" as used on page 38 of the application, or "antigen binding

fragment" a term substitution that would have been apparent to those in the art, would be more appropriate.

Appropriate correction is required.

4. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: there does not appear to be any antecedent basis support in the written description for the limitation in claim 17 specifying the domain at positions 481-683 of the matriptase protein. Applicant is requested to amend the application to provide such support.

It is noted that the application does refer to residues 432-683 of matriptase on page 64. However, there does not appear to be any identification of residue 481 as a specific end point for any fragment of the protein.

Note: this is not a written description rejection because the claim is an originally filed claim with the application, and thus the claims as filed provide support for the claimed subject matter. Amendment of the specification as indicated above would therefore not constitute new matter to the application.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 15-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims are drawn to an antibody or an "immunogenic fragment" thereof that binds to a matriptase protein. However, claim 19 further defines to the "immunogenic fragments" as antibody fragments known in the art to comprise antibody antigen binding domains. Thus, it is unclear if the Applicant meant to claim "immunogenic fragments," or meant to claim "immunologically reactive fragments," as a reading of the application (esp., page 38) and the substance of the claims would indicate.

Appropriate correction is required.

7. Claim 17 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim is rejected on two grounds.

First, this claim reads in part on antibodies that recognize and bind a domain located in amino acids 481-683 of SEQ ID NO: 5 or SEQ ID NO: 27. It is noted that the amino acids corresponding to residues 481-683 in the two identified sequences are not the same. It is therefore unclear if the Applicant intended to claim antibodies that bind to the residues corresponding to these positions in the mature form of the protein (SEQ ID NO: 5), or if the Applicant intended to refer to these positions on either SEQ ID NO: 5 or SEQ ID NO: 27.

Additionally, it is unclear what is meant by the phrase "as a region in the transmembrane domain." First, it appears that the Applicant intended to claim an antibody (or antigen binding fragment thereof) that binds - - to - - a region in the transmembrane domain. Second, there does

not appear to be any identification of which region (other than a suggestion that it may be near the C-terminus of the protein in Figure 14- without an identification of the specific region by amino acid positions). It is therefore unclear what is meant by "the transmembrane region."

Clarification is required.

8. Claims 17-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Each of these claims recites the limitation "the antibody of Claim 14." There is insufficient antecedent basis for this limitation in the claims because there is no antibody identified in claim 14.

It appears that the Applicant intended to identify the antibody of claim 15. It is therefore suggested that the claims be amended to depend from this claim.

For the purposes of this action, the claims are treated as though they depended from claim 15, rather than claim 14.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claim 16 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the

inventor(s), at the time the application was filed, had possession of the claimed invention. his claim is directed to any antibody (or fragment thereof) that can bind to the two-chain form of matriptase. The term matriptase is defined in the application as a "trypsin-like protein, with a molecular weight of between 72-kDa and 92-kDa and is related to SEQ ID NO: 27 or is a fragment thereof." Thus, the claims read on any antibody that binds to SEQ ID NO: 27, or to any related protein thereto.

The following quotation from section 2163 of the Manual of Patent Examination Procedure is a brief discussion of what is required in a specification to satisfy the 35 U.S.C. 112 written description requirement for a generic claim covering several distinct inventions:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus... See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.
>
> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Thus, when a claim covers a genus of inventions, the specification must provide written description support for the entire scope of the genus. Support for a genus is generally found where the applicant has provided a number of examples sufficient so that one in the art would recognize from the specification the scope of what is being claimed.

In the present case, the Applicant has identified only a single embodiment of a matriptase protein- that presented as SEQ ID NO: 5, or in mature form as SEQ ID NO: 27. However, as was indicated above, the term "matriptase" is defined in the application as reading on any "related" protein. It is not limited to the proteins of these two sequences. Additionally, the application also

noted that all known forms of matriptase are defined in Figure 14. The Applicant refers to these as "known forms" of matriptase, thereby indicating that the term "matriptase" is not limited to these forms. From this, it would appear that the Applicant is also claiming antibodies that bind to the human matriptase of SEQ ID NOs: 5 and 27, or to related proteins from other species.

The application nowhere provides any written description support for such other related forms of matriptase. There are neither a sufficient number of species of matriptase to support a claim to any matriptase, nor is there any identification of a common structure that does not vary from species to species. While the Applicant has defined a putative active sequence of 200 or more residues, the Applicant has not provided a common feature which is associated with any matriptase from any species. In view of the lack of examples of any matriptase other than the human form comprising one SEQ ID NOs: 5 or 27, or fragments thereof, the application has not provided adequate written description support for the full genus of any protein that is trypsin-like and "related" to SEQ ID NO: 27.

11. Claim 17 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This claim is directed in part to antibodies that bind to the transmembrane domain of matriptase. However, as was described above, the application has not provided a definition of what specific region of the protein corresponds to the indicated transmembrane domain. In view of this lack of

definition, the Applicant is attempting to claim a genus of antibodies identified only by their intended function- the ability to bind the transmembrane domain.

Means by which applicants may establish written description support for a claimed genus have been described above. In the present case, the application neither provides examples of antibodies that bind this region, which may be used as markers to identify further antibodies that bind to the same epitopes. Nor has the application provided any non-functional feature of the antibodies, such as the epitope targeted, or the region of matriptase defining the transmembrane domain. Because there is no such support for the claimed antibodies in the application, the claim is rejected as lacking adequate written description support.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

13. Claims 15 and16 are rejected under 35 U.S.C. 102(b) as being anticipated by Dickson et al. (U.S. Patent 5,482,848). These claims read on an antibody that binds to matriptase, and in particular to the two-chain form thereof. The application teaches that the two-chain form

corresponds to the proteins with an apparent size of 80-kDa isolated from T-47D breast cancer cells. Application, page 67.

Dickson teaches the use of such an 80-kDa protein to generate antibodies. Thus, the reference teaches the making and use of antibodies according to the claims.

14. Claims 15-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Lin et al. (J Biol Chem 272: 9147-52). These claims are directed to antibodies that bind to matriptase. As indicated above, the application teaches that the two-chain form corresponds to the proteins with an apparent size of 80-kDa isolated from T-47D breast cancer cells. The application additionally teaches that the region encompassing residues 432-683 of the protein appears to contain the active region of the protease. Page 66.

Lin teaches a monoclonal antibody that binds to such an 80 kDa protein. Abstract. In addition to these teachings, U.S. Patent 6,077,938 provides additional teachings regarding this antibody that indicate that the disclosed antibody was capable of binding somewhere in the active region of the protein. See e.g., column 3, lines 17-21, stating that the "isolated proteolytic activity corresponded to the polypeptides recognized by the mAb 21-9," and that "MAb 21-9 did not bind to the reduced protease." Thus, the Lin article anticipates the indicated claims.

15. Claims 15-18 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent 6,077,938. The claims have been described above.

Patent 6,077,938 teaches a monoclonal antibody, antibody 21-9, described as binding to the indicated 80-kDa protein. The teachings in column 3, lines 10-45, also indicate that the

disclosed antibody was capable of binding somewhere in the active region of the protein. See e.g., column 3, lines 17-21, stating that the "isolated proteolytic activity corresponded to the polypeptides recognized by the mAb 21-9," and that "MAb 21-9 did not bind to the reduced protease." Thus, the claims of the current application appear to be anticipated by those of the patent.

The applied reference has a common inventor and assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

16. Claims 15, 16, 18, and 19 are rejected under 35 U.S.C. 102(e) as being anticipated by O'Brien et al. (U.S. Patent 5,972,616). The claims have been described above. The patent teaches a protein referred to therein as TADG-15, and having the sequence identified in the patent as SEQ ID NO: 2. This protein has over 99% identity with the matriptase of SEQ ID NO: 27, as can be seen in the attached sequence alignment. In addition to teaching the protein, the patent also teaches antibodies that can bind thereto, and immunologically-active fragments of such antibodies. Column 9, lines 22-65. The reference therefore anticipates the indicated claims.

Claim Rejections - 35 USC § 103

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. Claim 18 rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over U.S. Patent 5,482,848 as applied above. This claim is directed to embodiments wherein the antibody is a monoclonal antibody. As indicated above, the patent teaches the making and use of antibodies directed against the 80kDa form of matriptase. However, in columns 6-7 of the patent, the patent teaches how polyclonal antibodies were made, but indicates that the hybridomas to make monoclonal antibodies "are started immediately" after the determination of matriptase binding by the antibodies. It is therefore unclear whether the reference actually teaches the making of monoclonal antibodies, or merely provides a predictive teaching of how to make them. Thus, the reference either anticipates, or renders obvious, the claimed antibodies.

19. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over any of U.S. Patents 5,482,848 or 6,077,938 (collectively- the Dickson patents), or Lin as applied to claims 15 and 16, or 15-18, above and further in view of McKenzie et al. (U.S. Patent 5,084,266) or Huang et al. (U.S. 5,516,637). Claim 19 is directed to embodiments of the claimed inventions wherein the invention comprises fragments of anti-matriptase antibodies, including Fab, $F(ab')_2$, and scFv molecules. The teachings of Lin and the Dickson patents have been described above. Each of

these references teaches the making and use of monoclonal antibodies against matriptase. However, they do not teach fragments thereof.

The teachings of each of the McKenzie (column 3) and Huang (column 6 lines 52-56) references indicate that it was known in the art that certain fragments of antibodies are functional equivalents of the antibodies themselves. It would therefore have been obvious to those in the art to construct such fragments of the anti-matriptase antibodies disclosed in Lin or the Dickson patents. The combined teachings of these references therefore render the claims obvious.

Double Patenting

20. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

21. Claims 15-18 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9 of U.S. Patent No. 6,077,938. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the patent are drawn to the monoclonal antibody 21-9 (described above). Because the claims of the parent application anticipate the current claims as a species of the currently

claimed genus if applied as prior art (see above), the present claims are rejected as being obvious thereto. See MPEP 806.04(i).

22. Claims 15, 16, and 18 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 4 and 5 of U.S. Patent 5,482,848. The claims of the patent read on compositions including an antibody against matriptase. Thus, the claims of the prior patent represent a species of the claimed genus. The claims are therefore rejected for obvious type double patenting over the claims of the parent application. See e.g., MPEP 806.04(i).

23. Claim 19 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim1-9 of U.S. Patent 6,077,938 or of claims 4 and 5 of U.S. Patent No. 5,482,848, further in view of either McKenzie or Huang as described above. As indicated above, the claims of the prior Dickson patents provide a basis for obviousness type double patenting rejection of claims 15-18 of the present claims. However, neither the teachings nor the claims of these patents render obvious the making and use of the fragments of anti-matriptase antibodies claimed in claim 19.

However, as described above, the teachings of McKenzie and Huang indicate that it was accepted in the art that certain fragments of antibodies are functional equivalents thereof. Thus, it would have been obvious to those in the art to substitute such fragments for the antibodies in the claims of the Dickson patents. Claim 19 is therefore rejected as an obvious variation of the claims of the Dickson patents for the reasons indicated above, both as to the claims of the

Dickson patents, and in the obviousness rejection of claim 19 under 35 U.S.C. 103(a) over these references above.

Conclusion

24. No claims are allowed.

25. The following prior art references are made of record and considered pertinent to applicant's disclosure. However, while relevant they are also not used as a basis for rejection for the stated reasons.

> O'Brien et al., Tumor Biol 19(S2): 33 and Tanimoto et al., Proceedings of the American Association for Cancer Research Annual Meeting, 1998 39: 648. Each of these references teach a serine protease identified as TADG-15 as a marker for ovarian cancer. Thus, if these references were enabling for the TADG-15 protein, they would render the claimed inventions obvious when combined with McKenzie et al. (U.S. 5,084,266), which teaches the use of antibodies directed against cancer markers. However, while the TADG-15 protein was later disclosed (See e.g., O'Brien et al., U.S. Patent 5,972,616) as a protein sharing over 99% identity with matriptase, neither of the O'Brien or Tanimoto articles provide any means by which those in the art could make and use the protein. The references merely provide a name, a protein length, and identify cells from which they were identified. However, there is no disclosure of any sequence (gene or protein) or identification of the probes or primers used in the PCR methods by which the protein was identified. Because the references do not enable the use of the protein, they are not applied as art against the present claims.

26. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas
Patent Examiner

James C. Housel 1/24/05

JAMES HOUSEL
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600